REMARKS

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

The Invention

Applicants' invention comprises, *inter alia*, human DnaJ-like proteins (hereinafter referred to as HSPJ1 and HSPJ2, and collectively, as HSPJ), the polynucleotides encoding HSPJ, and variants thereof for the diagnosis of acquired and inherited disease, expression profiling, and drug development. HSPJ are human homologues of the DnaJ component of the bacterial Hsp70 heat shock protein complex (DnaK/DnaJ/GrpE), a well characterized bacterial chaperone used as a model for eukaryotic cellular chaperones. Applicants' invention is described in detail throughout the specification of the above identified application.

Amendments to Claims

Claims 43-61 and 65-68 are pending in the above identified application. Claims 45-49, 52-56, and 65 (Group II) were provisionally elected by verbal restriction. Claims 66-68 were newly added in the amendment filed September 25, 2000. Claim 53 is canceled, without prejudice, by this amendment. Claim 49 was objected to as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim from which it depends (Office Action, paragraph bridging pages 2-3). Claim 49 has been rewritten to address this objection. It is therefore requested that this objection be withdrawn.

Written description rejections under 35 U.S.C. § 112, first paragraph

Claims 45, 47-49, 52-56, and 66-68 have been rejected under the first paragraph of 35 U.S.C. 112 for alleged lack of an adequate written description. This rejection is respectfully traversed.

Claim 53 has been canceled by this amendment, and claim 49 has been amended to remove language reciting biologically-active and immunogenic fragments of SEQ ID NO:1 and SEQ ID NO:3. Hence, various issues pertaining to claims 53 and 49 are rendered moot.

Remaining issues are discussed below.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art. SEQ ID NO:1 and SEQ ID NO:3 are specifically disclosed in the application (see, for example, page 15, line 20 through page 16, line 19). Polypeptide variants having at least 90% identity to SEQ ID NO:1 and SEQ ID NO:3 are described, for example, at page 16, lines 20-23. Accordingly, the Specification provides an adequate written description of the recited polypeptide sequences.

Additionally, the Office Action has asserted that the claims are "...drawn to a vast diverse genus of a DNA encoding a polypeptide comprising...at least 16, 20, 30 or 60 contiguous nucleotides of said sequences..." and that the "...specification does not disclose structural, physico-chemical or biological characteristics of a polypeptide comprising...at least 16, 20, 30 or 60 contiguous nucleotides." This position appears to be based, at least in part, on a misstatement of what is recited by the claims. That is, claims 54 and 67 recite a ***method for detecting a target***

polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 52 (that is, for example, a) a polynucleotide sequence of SEQ ID NO:2 or SEQ ID NO:4, b) a naturally-occurring polynucleotide sequence having at least 90% sequence identity to the sequence of SEQ ID NO:2 or SEQ ID NO:4, c) a polynucleotide sequence complementary to a), or d) a polynucleotide sequence complementary to b)) wherein a probe comprising at least 16 (or, for example, 20 or 30 or 60) contiguous nucleotides comprising a sequence complementary to said target polynucleotide is utilized in the detection of said target polynucleotide in a sample. Comparable language is found in claim 66. Clearly, these contiguous nucleotides are intended to be used in this method as probes to detect complimentary polynucleotide sequences in a sample. Support for such use of nucleic acid sequences of this type can be found, for example, in the Specification at page 13, lines 9-13. Their structure is defined by the portion of the target polynucleotide to which they bind (for example, SEQ ID NO:2 or SEQ ID NO:4, both of which are specifically disclosed in the application, for example, in the Specification at page 16, lines 24-29); and their function is to bind to the complimentary portion of the target polynucleotide in the sample. As such, both their structure and function are defined in the Specification; and the written description is fully adequate in this regard.

A. The Specification provides an adequate written description of the claimed "variants" of SEQ ID NO:1 and SEQ ID NO:3.

The Office Action has further asserted that the claims are not supported by an enabling disclosure because "[t]he specification does not contain any disclosure of the function of all DNA sequences that are 90% identical to SEQ ID NOs:2 or 4" (page 5 of the Office Action at June 21, 2000). It should be noted, however, that knowledge of the precise biological role of any or all of the proteins encoded for by the recited polynucleotides is unnecessary. Rather, it is sufficient that the claimed polynucleotides can be used in any one disclosed or well known use, such as toxicology testing, drug discovery, and the diagnosis of disease. The present Specification provides an adequate written description for such uses.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of functional features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant phasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court

therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides in terms of chemical structure, rather than on functional characteristics. For example, the "variant language" of independent claim 45 recites chemical structure to define the claimed genus:

> 45. An isolated polynucleotide encoding . . . a) a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 or SEQ ID NO:3. . .

Comparable language is found in independent claim 52, which refers to the polynucleotide sequences of SEQ ID NO:2 or SEQ ID NO:4.

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1 or SEQ ID NO:3. In the present case, there is no reliance merely on a description of functional characteristics of the claimed polynucleotides. In fact, there is no recitation of functional characteristics. Moreover, if such functional recitations were included, it would add to the structural characterization of the claimed polynucleotides. The polynucleotides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims to nucleic acids. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as

"highly variant." Available evidence illustrates that, rather than being highly variant, the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <40% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The present application is directed, *inter alia*, to DNAJ-like polypeptides related to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3. In accordance with Brenner et al, naturally occurring molecules may exist which could be characterized as DNAJ-like polypeptides and which have as little as 40% identity over at least 70 residues to SEQ ID NO:1 or SEQ ID NO:3. The "variant language" of the present claims recites, for example, "a polynucleotide encoding a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 or SEQ ID NO:3" (note that SEQ ID NO:1 has 358 amino acid residues and SEQ ID NO:3 has 330 amino acids). This variation is far less than that of all potential DNAJ-like polypeptides related to SEQ ID NO:1 or SEQ ID NO:3, i.e., those DNAJ-like polypeptides having as little as 30% identity over at least 150 residues to SEQ ID NO:1 or SEQ ID NO:3.

The case of *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) provides further support for concluding that the polypeptide genus defined by the present claims complies with the written description requirement. As discussed above, certain claims of U.S. Patent No. 4,652,525 were found invalid for failing to satisfy the written description requirement. The *Lilly* case, however, also considered U.S. Patent No. 4,431,740. While there is a discussion in *Lilly* of issues of infringement and enforceability of the claims of the '740 patent, there is no written description analysis of the claims of the '740 patent. However, there was no

holding of invalidity of any claim of the '740 patent. Thus, the claims of the '740 patent are presumed to satisfy the written description of 35 U.S.C. §112. See 35 U.S.C. §282. Now consider, for example, claim 4 of the '740 patent, which reads as follows:

> 4. A DNA transfer vector comprising a deoxynucleotide sequence coding for human pre-proinsulin consisting essentially of a plus strand having the sequence:

5'-$_{-24}$ GCL$_{-23}$ X$_{-22}$ TY$_{-22}$ TGG-$_{21}$ ATG$_{-20}$ W$_{-19}$ GZ$_{-19}$ X$_{-18}$ TY$_{-18}$ X$_{-17}$ TY$_{-17}$ CCL$_{-16}$ X$_{-15}$TY$_{-15}$ X$_{-14}$ TY$_{-14}$ GCL$_{-13}$ X$_{-12}$ TY$_{-12}$ X$_{-11}$ TY$_{-11}$ GCL$_{-10}$ X$_{-9}$ TY$_{-9}$ TGG$_{-8}$ GGL$_{-7}$ CCL$_{-6}$GAK$_{-5}$ CCL$_{-4}$ GCL$_{-3}$ GCL$_{-2}$ GCL$_{-1}$ TTK$_1$ GTL$_2$ AAK$_3$ CAJ$_4$ CAK$_5$ X$_6$ TY$_6$ TGK$_7$ GGL$_8$ QR$_9$ S$_9$ CAK$_{10}$ X$_{11}$ TY$_{11}$ GTL$_{12}$ GAJ$_{13}$ GCL$_{14}$ X$_{15}$ TY$_{15}$ TAK$_{16}$ X$_{17}$ TY$_{17}$ GTL$_{18}$ TGK$_{19}$ GCL$_{20}$ GAJ$_{21}$ W$_{22}$ GZ$_{22}$ GCL$_{23}$ TTK$_{24}$ TTK$_{25}$ TAK$_{26}$ ACL$_{27}$ CCL$_{28}$ AAJ$_{29}$ ACL$_{30}$ W$_{31}$ GZ$_{31}$ W$_{32}$ GZ$_{32}$ GAJ$_{33}$ GCL$_{34}$ GAJ$_{35}$ GAK$_{36}$ X$_{37}$ TY$_{37}$ CAJ$_{38}$ GTL$_{39}$ GGL$_{40}$ CAJ$_{41}$ GTL$_{42}$ GAJ$_{43}$ X$_{44}$ TY$_{44}$ GGL$_{45}$ GGL$_{46}$ GGL$_{47}$ CCL$_{48}$ GGL$_{49}$ GCL$_{50}$ GGL$_{51}$ QR$_{52}$ S$_{52}$ X$_{53}$ TY$_{53}$ CAJ$_{54}$ CCL$_{55}$ X$_{56}$ TY$_{56}$ GCL$_{57}$ X$_{58}$ TY$_{58}$ GAJ$_{59}$ GGL$_{60}$ QR$_{61}$ S$_{61}$ X$_{62}$ TY$_{62}$ CAJ$_{63}$ AAJ$_{64}$ W$_{65}$ GZ$_{65}$ GGL$_{66}$ ATM$_{67}$ GTL$_{68}$ GAJ$_{69}$ CAJ$_{70}$ TGK$_{71}$ TGK$_{72}$ ACL$_{73}$ QR$_{74}$ S$_{74}$ ATM$_{75}$ TGK$_{76}$ QR$_{77}$ S$_{77}$ X$_{78}$ TY$_{78}$ TAK$_{79}$ CAJ$_{80}$ X$_{81}$ TY$_{81}$ GAJ$_{82}$ AAK$_{83}$ TAK$_{84}$ TGK$_{85}$ AAK$_{86}$ TAGACGCAGCCCGCAGGCAGCCCCCCACCCGCCGCCTCCTGCACCGAGAGAGATGG AATAAAGCCCTTGAACCA GC polyA-3'

> wherein
>
> A is deoxyadenyl,
>
> G is deoxyguanyl,
>
> C is deoxycytosyl,
>
> T is thymidyl,
>
> J is A or G;
>
> K is T or C;
>
> L is A, T, C, or G;
>
> M is A, C or T;
>
> X_n is T or C if Y_n is A or G; and C if Y_n is C or T;
>
> Y_n is A, G, C or T if X_n is C, and A or G if X_n is T;
>
> W_n is C or A if Z_n is G or A, and C if Z_n is C or T;
>
> Z_n is A, G, C or T if W_n is C, and A or G if W_n is A;
>
> QR_n is TC if S_n is A, G, C or T, and AG if S_n is T or C;

S_n is A, G, C or T if QR_n is TC, and T or C if QR_n is AG; and, script numerals, n, refer to the position in the amino acid sequence of human proinsulin, to which each triplet in the nucleotide sequence corresponds, according to the genetic code, the amino acid positions being numbered from the amino end.

Claim 4 of the '740 patent recites a DNA sequence with includes the coding region for human pre-proinsulin; in particular, the 330 nucleotide bases from codon $-GCL_{24}$ through codon AAK_{86} code for human pre-proinsulin. As can be seen from the claim language, claim 4 of the '740 patent sets forth a DNA structure with numerous variant positions. Of the 330 nucleotides in the coding region for human pre-proinsulin, 141 are potentially variant positions within the structure defined by claim 4. Thus, claim 4 of the '740 patent defines a DNA which potentially is only 57% identical (189/330 x 100% = 57%) to the single species of human pre-proinsulin actually sequenced in the '740 patent. See Example 1 and Figure 2. As discussed above, the present claims encompass polynucleotides encoding naturally-occurring polypeptide variants which have at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3. Clearly, then, the genus variation of the present claims is less than that of claim 4 of the '740 patent.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of June 3, 1997. Much has happened in the development of recombinant DNA technology in the 20 or so years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been

compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, and SEQ ID NO:4, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application.

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:4. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids. In addition, the genus of polynucleotides defined by the present claims is not "highly variant," as evidenced by Brenner et al and consideration of the claims of the '740 patent involved in *Lilly*. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

For at least the above reasons, withdrawal of these rejections is requested.

Enablement rejections under 35 U.S.C. § 112, first paragraph

Claims 49, 53-56, and 66 have been rejected under 35 U.S.C.§112, first paragraph as allegedly being based on a disclosure which does not provide enablement commensurate in scope with the claims. This rejection is traversed as well.

According to the Office Action, the claims drawn to a DNA encoding a polypeptide comprising sequences 90% identical to SEQ ID NO:1 or SEQ ID NO:3 are not supported by an enabling disclosure because, among other things, the specification allegedly "...provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful." The Office Action appears to be misguided, at least in part, by ignoring the claim

recitation of a "***naturally-occurring amino acid sequence*** having at least 90% sequence identity to the sequence of SEQ ID NO:1 or SEQ ID NO:3" In this regard, see comments in the Office Action at page 6 such as "regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention", "the general tolerance of said polypeptide to modification and extent of such tolerance" and "a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function." Such issues are simply not relevant to naturally-occurring polypeptides.

Additionally, the Specification describes how to make and use polypeptides comprising "a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 or SEQ ID NO:3." See, *e.g.*, the Specification at pages 15 to 16 for a description of the amino acid sequences of SEQ ID NO:1 and SEQ ID NO:3, and the polynucleotide sequences encoding the polypeptides (i.e., SEQ ID NO:2 and SEQ ID NO:4). See also page 16, lines 20-23 for a description of variants of HSPJ. When provided with the present disclosure, such naturally-occurring sequences can be routinely identified by one of skill in the art.

With respect to the enablement rejection regarding claims drawn to a DNA "... comprising at least 16, 20, 30 or 60 contiguous nucleotides of said sequences...", it is clear from the claims that these sequences are intended to be used as probes in ***a method for detecting a target polynucleotide in a sample***, as discussed above in the section regarding the written description issues. Again, support for such use of nucleic acid sequences of this type can be found, for example, in the Specification at page 13, lines 9-13. In this regard, one of skill in the art would be able to practice the invention with no further guidance.

For at least the foregoing reasons, withdrawal of these rejections is requested.

The rejections under 35 U.S.C. § 112, second paragraph

Claims 49, 65, 67, and 68 stand rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness.

Claim 49 has been amended to remove the recitation of a "biologically-active fragment"; hence this issue is moot.

According to the Office Action, claims 65, 67, and 68 are incomplete for omitting essential elements. In particular, the Office Action has asserted that "...in claims 65 and 68, a

probe used for detecting is not defined..." Such is not the case, however. Note, for example, the Specification at page 41, line 13 through page 42, line 4, which describes methods for screening a compound for effectiveness in altering expression of a target polynucleotide. Such methods are well known to those of skill in the art and are routinely used in such screening procedures. Additional support for these methods can be found, for example, in the Specification at page 43, lines 1-28. Any of these descriptions provides the basis for completeness with respect to claims 65 and 68.

The Office Action has further asserted that claim 67 is allegedly incomplete because "...compounds used in polymerase chain reaction are not defined." Such, however, is not the case. Note, for example, the Specification at page 9, lines 5-8, which defines "Amplification" as "...the production of additional copies of a nucleic acid sequence...generally carried out using polymerase chain reaction (PCR) technologies ***well known in the art***..." Furthermore, a reference is given for a laboratory manual which describes these procedures, including the compounds used therein, in detail. Thus, compounds used in polymerase chain reaction are both described in the Specification and well known in the art. Therefore, a detailed recitation of such components by the claims is unnecessary.

For at least the foregoing reasons, it is requested that these rejections be withdrawn.

The rejections under 35 U.S.C. § 102

Claims 45, 52, and 53 stand rejected under 35 U.S.C. 102(a) as being anticipated by any of the Hillier et al. documents (N93316, W63690, and AA020916). Claim 53 has been canceled. These rejections, as they apply to claims 45 and 52, are respectfully traversed.

It is believed that the rejections over the Hillier et al. documents are based on a misinterpretation of the claims. That is, the recitation of "a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 or SEQ ID NO:3" means that one must make a comparison across the full length of SEQ ID NO:1 or SEQ ID NO:3.

Accession No. N93316 describes a polynucleotide sequence which has 34.7% identity to SEQ ID NO:2 over the entire length of SEQ ID NO:2 (478 out of 1376 nucleotides). Accession No. W63690 describes a polynucleotide sequence which has 42% identity to SEQ ID NO:4 over the entire length of SEQ ID NO:4 (559 out of 1330 nucleotides). Accession No. AA020916

describes a polynucleotide sequence which has 43.7% identity to SEQ ID NO:4 over the entire length of SEQ ID NO:4 (582 out of 1330 nucleotides). Furthermore, N93316, W63690, and AA020916 are ESTs and there is no indication of an "encoded fragment." Moreover, none of these records provides an indication of an appropriate reading frame or start codon. Clearly, then, N93316, W63690, and AA020916 are not pertinent to the present application. For at least the above reasons, withdrawal of the §102 rejections is requested.

Double Patenting

Claims 45-49, 52, and 53 stand rejected under the judicially created doctrine of double patenting over claims 1-9 of U. S. Patent No. 5,922,567 and claims 1-9 of U.S. Patent No. 6,001,598. It is requested that the requirement for submission of a terminal disclaimer be held in abeyance until such time as there is an indication of one or more allowable claims.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present claims define allowable subject matter, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650)855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108. This form is enclosed in duplicate.**

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 53 has been canceled.

Claim 49 has been amended as follows:

49. **(Amended)** A method for producing a polypeptide selected from the group consisting of:

[i)]a) an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, and

[ii)]b) a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 or SEQ ID NO:3,

[iii) a biologically-active fragment of the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, and

iv) an immunogenic fragment of the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3,]

the method comprising:

[a)]i) culturing a cell of claim 48 under conditions suitable for expression of the polypeptide, and

[b)]ii) recovering the polypeptide so expressed.